CLAIMS

We claim:

1. A dual release drug delivery device comprising:

a first composition comprising a therapeutically effective amount of an antiviral neuraminidase inhibitor and at least one pharmaceutical excipient; and

a different second composition comprising a therapeutically effective amount of an H1 histamine receptor antagonist;

wherein the first composition provides a controlled, extended, retarded and/or sustained release of the antiviral neuraminidase inhibitor and the second composition provides a rapid and/or immediate release of an H1 histamine receptor antagonist.

2. The device of claim 1, wherein the device is selected from the group consisting of capsules containing immediate and sustained release granules, capsules containing sustained release granules and one or more immediate release tablets, capsules containing sustained release granules and powder, extended release film or multi-layer coated tablets.

3. The device of claim 2, wherein at least 75% of the H1 antagonist is released within about 120 minutes and at least about 70% of the antiviral neuraminidase inhibitor is released within about 24 hours after exposure of the device to an aqueous environment.

4. The device of claim 2, wherein the first drug composition further comprises at least one release rate modifier.

5. The device of claim 2, wherein the second drug composition further comprises at least one pharmaceutical excipient.

6. The device of claim 2, wherein the first and second drug compositions are in layered arrangement with respect to one another.

7. The device of claim 2, wherein the second drug composition surrounds the first drug composition.

8. The device of claim 6 or 7, wherein the first drug composition is in contact with the second drug composition.

9. The device of claim 6 or 7, wherein the first drug composition is spaced-away from the second drug composition.

10. The device of claim 6 or 7, wherein the first drug composition is included in a core and the second drug composition is included in a coat, of one or more coats, surrounding the core.

11. The device of claim 1, wherein the first drug composition is a granulation, the second drug composition is a powder, granulation or compressed tablet and the device is a capsule.

12. A dual release osmotic device comprising:

a core comprising a therapeutically effective amount of an antiviral neuraminidase inhibitor and at least one osmotic agent or osmopolymer, wherein the core provides a controlled release of the neuraminidase inhibitor;

a semipermeable membrane surrounding the core and having a passageway there through; and

a drug-containing coat comprising a therapeutically effective amount of an H1 antagonist and surrounding the semipermeable membrane, wherein the external coat provides a rapid release of the H1 antagonist.

13. The osmotic device of claim 12, wherein the osmotic device further comprises an inert water soluble or erodible coat interposed the semipermeable membrane and the drug-containing coat.

14. The osmotic device of claim 13, wherein the drug-containing water soluble or erodible coat is sprayed onto the inert water soluble coating.

15. The osmotic device of claim 12, wherein the osmotic device further comprises one or more other coats surrounding the core.

16. The osmotic device of claim 15, wherein the one or more coats are selected from the group consisting of inert water-soluble coat, inert water-erodible coat, immediate release coat, rapid release coat, and delayed release coat.

17. The osmotic device of claim 12, wherein the neuraminidase inhibitor is released in a controlled or sustained manner over a period of about 20-24 hours after exposure to an aqueous environment, and the H1 antihistamine is released over a period of about 15-120 minutes after exposure to an aqueous environment.

18. The osmotic device of claim 17, wherein 70-100% of the neuraminidase inhibitor is released within 23 hours after exposure to an aqueous environment.

19. The osmotic device of claim 12, wherein the H1 antagonist is selected from the group consisting of acrivastine, astemizole, azelastine, cetirizine, ebastine, epinastine, fexofenadine, desloratadine, loratadine, mizolastine, norastemizole, prometazine and terfenadine.

20. The osmotic device of claim 19, wherein the device provides an antiviral neuraminidase inhibitor dissolution profile approximately as follows when exposed to an aqueous environment:

Time (h)	Maximum released (%)	Minimum released (%)
3	30	5
7	64	27
11	84	48
15	95	62
23	100	74

21. The osmotic device of claim 20, wherein the device provides an H1 antagonist dissolution profile approximately as follows when exposed to an aqueous environment.:

Time (min)	Minimum Released (%)	Maximum Released (%)
15	24	94
30	40	100
45	60	100
60	80	100
120	100	

22. A combination rapid release and controlled release device comprising:

(a) a core comprising a therapeutically effective amount of an antiviral neuraminidase inhibitor which is delivered at a controlled rate over a period of at least about 18-24 hours;

(b) a semipermeable membrane surrounding the core and a passageway through the semipermeable membrane;

(c) an inert water soluble or erodible coating surrounding the semipermeable membrane and plugging the passageway; and

(d) an H1 antagonist-containing water soluble coating surrounding the inert water soluble coating for delivering all of the H1 antagonist at a rapid rate over a period of less than about 120 min.

23. The device of claim 22, wherein about 75 - 800 mg of the neuraminidase inhibitor and about 2.5 - 180 mg of H1 antagonist are present.

24. The device of claim 22, wherein:

the core further comprises an osmagent, a diluent and a binder;

the semipermeable membrane comprises a cellulose ester and a plasticizer;

the inert water soluble or erodible coating comprises a water soluble polymer, an opaquant and a filler; and

the H1 antagonist-containing water soluble coating further comprises a film forming polymer and a disintegrant.

25. The controlled release device of claim 24, wherein:

the osmagent is selected from the group consisting of sodium chloride, salt, mannitol, acid, sugar, base, calcium salt, sodium salt, and lactose;

the diluent is selected from the group consisting of microcrystalline cellulose, lactose, sucrose, mannitol, cellulose, starch, sorbitol, dibasic calcium phosphate, and calcium carbonate;

the binder is selected from the group consisting of poly(vinylpyrrolidone), povidone, sodium carboxymethylcellulose, alginic acid, poly(ethylene glycol), guar gum, polysaccharide, bentonite clay, sugar, poloxamer, collagen, albumin, gelatin, poly(propylene glycol), and poly(ethylene oxide);

the cellulose ester is selected from the group consisting of cellulose acetate, cellulose acylate, cellulose fatty acid ester, and cellulose acetate phthalate;

the plasticizer is independently selected at each occurrence from the group consisting of poly(ethylene glycol), low molecular weight polymer, citrate ester, triacetin, propylene glycol, glycerin, sorbitol lactate, ethyl lactate, butyl lactate, ethyl glycolate, and dibutylsebacate;

the water soluble polymer is independently selected at each occurrence from the group consisting of hydroxypropyl methylcellulose, poly(vinlypyrrolidone)-(vinyl acetate) copolymer, poly(vinylpyrrolidone), methyl methacrylate, calcium pectinate,

poly(ethylene-vinyl acetate), hydroxylalkyl alkylcellulose, polyvinylalcohol, polyethylene oxide, a blend of gelatin and polyvinyl-pyrrolidone, gelatin, glucose, saccharide, povidone, copovidone, and polysaccharide gum;

the opaquant is selected from the group consisting of titanium dioxide and talc;

the filler is selected from the group consisting of talc and starch;

the film forming polymer is selected from the group consisting of hydroxypropyl methylcellulose, and poly(vinylpyrrolidone); and

the disintegrant is selected from the group consisting of crospovidone, bentonite clay, microcrystalline cellulose, starch, carboxymethylcellulose, alginate, sodium starch glycolate, and gum.

26. The device of claim 25, wherein:

the opaquant is selected from the group consisting of titanium dioxide and talc; and

the filler is selected from the group consisting of talc and starch.

27. The device of claim 24, wherein:

the osmagent is present in an amount ranging from 45 - 155 mg;

the diluent is present in an amount ranging from 0 - 100 mg;

the binder is present in an amount ranging from 20 - 60 mg;

the cellulose ester is present in an amount ranging from 20 – 50 mg;

the film-forming polymer in the H1 antagonist-containing water soluble coating is present in an amount ranging from 20 – 40 mg; and

the disintegrant in the H1 antagonist-containing water soluble coating is present in an amount ranging from 100 - 200 mg.

28. A dual release capsule comprising:

a first composition consisting essentially of plural granules comprising a therapeutically effective amount of an antiviral neuraminidase inhibitor and at least one pharmaceutical excipient; and

a different second composition comprising a therapeutically effective amount of an H1 histamine receptor antagonist;

wherein the first composition provides a controlled or sustained release of the antiviral neuraminidase inhibitor and the second composition provides a rapid release of an H1 histamine receptor antagonist.

29. The capsule of claim 28, wherein the first composition is a granulation and the second composition is a powder, granulation or one or more tablets.

30. The capsule of claim 29, wherein the H1 antagonist is selected from the group consisting of acrivastine, astemizole, azelastine, cetirizine, ebastine, epinastine, fexofenadine, loratadine, mizolastine, norastemizole, desloratadine, prometazine and terfenadine.

31. The capsule of claim 28, wherein the neuraminidase inhibitor is selected from the group consisting of zanamivir, peramivir, (+/-)-(2S,3R,4R)-2-(trifluoroacetamido)methyl-3-amino-1-(N'-ethyl-N'-isopropylcarbamyl)pyrrolidine-4-carboxylic acid and 4-(acetylamino)-3-hydroxy-5-nitrobenzoic acid.

32. The delivery device of claim 1, wherein the neuraminidase inhibitor is selected from the group consisting of zanamivir, peramivir, (+/-)-(2S,3R,4R)-2-(trifluoroacetamido)methyl-3-amino-1-(N'-ethyl-N'-isopropylcarbamyl)pyrrolidine-4-carboxylic acid and 4-(acetylamino)-3-hydroxy-5-nitrobenzoic acid.

33. The osmotic device of claim 12, wherein the neuraminidase inhibitor is selected from the group consisting of zanamivir, peramivir, (+/-)-(2S,3R,4R)-2-(trifluoroacetamido)methyl-3-amino-1-(N'-ethyl-N'-isopropylcarbamyl)pyrrolidine-4-carboxylic acid and 4-(acetylamino)-3-hydroxy-5-nitrobenzoic acid.

34. The device of claim 22, wherein the neuraminidase inhibitor is selected from the group consisting of zanamivir, peramivir, (+/-)-(2S,3R,4R)-2-(trifluoroacetamido)methyl-3-amino-1-(N'-ethyl-N'-isopropylcarbamyl)pyrrolidine-4-carboxylic acid and 4-(acetylamino)-3-hydroxy-5-nitrobenzoic acid.

35. A dual release drug delivery device comprising:

an antiviral neuraminidase inhibitor selective for neuraminidase A or B, wherein the inhibitor is present in controlled, sustained, extended or prolonged release form;

an H1 antihistamine receptor antagonist present in rapid release form such that it is substantially completely released within two hours after exposure of the device to an aqueous environment; and

at least one pharmaceutical excipient.

36. The device of claim 35, wherein the neuraminidase inhibitor is selected from the group consisting of zanamivir, peramivir, (+/-)-(2S,3R,4R)-2-

(trifluoroacetamido)methyl-3-amino-1-(N'-ethyl-N'-isopropylcarbamyl)pyrrolidine-4-carboxylic acid and 4-(acetylamino)-3-hydroxy-5-nitrobenzoic acid, and the H1 antihistamine receptor antagonist is selected from the group consisting of acrivastine, astemizole, azelastine, cetirizine, ebastine, epinastine, fexofenadine, desloratadine, loratadine, mizolastine, norastemizole, prometazine and terfenadine.

37. The device of claim 36 further comprising a bioabsorption enhancer that enhances the absorption of the neuraminidase inhibitor across the lining of the gastrointestinal tract when the device is administered orally to a subject.

38. The device of claim 37, wherein the bioabsorption enhancer is selected from the group consisting of vitamin E TPGS, acetylated monoglyceride citric acid, malic acid, ascorbic acid, fumaric acid, caproic acid, caprylic acid, cholic acid, glycocholic acid, sodium cholate, sodium lauryl sulfate, palmitoyl carnitin, or a mixture thereof.

39. The device of claim 35, 36 or 37, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	Average (%)	STD ±(%)
0	0	0
4	17	5.0
8	45	5.0
12	65	6.0
16	77	5.0
24	90	4.0

40. The device of claim 35, 36 or 37, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	STD ±(%)	RANGE (%)	
		MAX	MIN
0	0	0	0
4	5.0	35	5
8	5.0	65	25
12	6.0	87	48
16	5.0	99	60
24	4.0	100	70

41. The device of any one of claim 1-4, 6-7, or 11, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	Average (%)	STD ±(%)
0	0	0
4	17	5.0
8	45	5.0
12	65	6.0
16	77	5.0
24	90	4.0

42. The device of any one of claim 1-4, 6-7, or 11, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	STD ±(%)	RANGE (%)	
		MAX	MIN
0	0	0	0
4	5.0	35	5
8	5.0	65	25
12	6.0	87	48
16	5.0	99	60
24	4.0	100	70

43. The device of any one of claim 12-13, 15-18 or 19, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	Average (%)	STD ±(%)
0	0	0
4	17	5.0
8	45	5.0
12	65	6.0
16	77	5.0
24	90	4.0

44. The device of any one of claim 12-13, 15-18 or 19, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	STD ±(%)	RANGE (%)	
		MAX	MIN
0	0	0	0
4	5.0	35	5
8	5.0	65	25
12	6.0	87	48
16	5.0	99	60
24	4.0	100	70

45. The device of any one of claim 22-24, or 27, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	Average (%)	STD ±(%)
0	0	0
4	17	5.0
8	45	5.0
12	65	6.0
16	77	5.0
24	90	4.0

46. The device of any one of claim 22-24, or 27, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	STD ±(%)	RANGE (%)	
		MAX	MIN
0	0	0	0
4	5.0	35	5
8	5.0	65	25
12	6.0	87	48
16	5.0	99	60
24	4.0	100	70

47. The capsule of any one of claim 28-30 or 31, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	Average (%)	STD ±(%)
0	0	0
4	17	5.0
8	45	5.0
12	65	6.0
16	77	5.0
24	90	4.0

48. The capsule of any one of claim 28-30 or 31, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	STD ±(%)	RANGE (%)	
		MAX	MIN
0	0	0	0
4	5.0	35	5
8	5.0	65	25
12	6.0	87	48
16	5.0	99	60
24	4.0	100	70

49. The capsule of any one of claim 32, 33 or 34, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	Average (%)	STD ±(%)
0	0	0
4	17	5.0
8	45	5.0
12	65	6.0
16	77	5.0
24	90	4.0

50. The capsule of any one of claim 32, 33 or 34, wherein the neuraminidase inhibitor is released according to the following profile after exposure to an aqueous environment:

Time after Exposure (hrs)	STD ±(%)	RANGE (%)	
		MAX	MIN
0	0	0	0
4	5.0	35	5
8	5.0	65	25
12	6.0	87	48
16	5.0	99	60
24	4.0	100	70